Amendments to the Specification:

Please replace the paragraph beginning at page 42, line 12, with the following redlined paragraph:

T cells may be stimulated with WT1 polypeptide, polynucleotide encoding a WT1 polypeptide and/or an antigen presenting cell (APC) that expresses a WT1 polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the WT1 polypeptide. Preferably, a WT1 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of antigen-specific T cells. Briefly, T cells, which may be isolated from a patient or a related or unrelated donor by routine techniques (such as by ~~Ficoll~~FICOLL®/~~Hypaque~~ HYPAQUE® density gradient centrifugation of peripheral blood lymphocytes), are incubated with WT1 polypeptide. For example, T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with WT1 polypeptide (*e.g.,* 5 to 25 μg/ml) or cells synthesizing a comparable amount of WT1 polypeptide. It may be desirable to incubate a separate aliquot of a T cell sample in the absence of WT1 polypeptide to serve as a control.

Please replace the paragraph beginning at page 55, line 28, with the following redlined paragraph:

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A (MPL®), preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL™), together with an aluminum salt. MPL® adjuvants are available from Corixa Corporation (Seattle, WA; *see*, for example, US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science 273*:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila

Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins . Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example combinations of at least two of the following group comprising QS21, QS7, Quil A, β-escin, or digitonin.

Please replace the paragraph beginning at page 56, line 15, with the following redlined paragraph:

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix, particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOM®s. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or suspension, or in a particulate structure such as a paucilamelar liposome or ISCOM®. The saponins may also be formulated with excipients such as ~~Carbopol®~~ CARBOPOL® to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

Please replace the paragraph beginning at page 57, line 10, with the following redlined paragraph:

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include ~~Montanide~~ MONTANIDE® ISA 720 (Seppic, France), SAF™ (Chiron, California, United States), ISCOM®~~S~~s (CSL), MF-59™ (Chiron), the SBAS™ series of adjuvants (*e.g.,* SBAS™-2 or SBAS™-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (~~Enhanzyn~~ENHANZYN®) (Corixa, Hamilton, MT), RC-529™ (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the

disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Please replace the paragraph beginning at page 80, line 1, with the following redlined paragraph:

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or ~~Tween~~ TWEEN® 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of WT1 polypeptide within a sample obtained from an individual with a cancer associated with WT1 least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Please replace the paragraph beginning at page 80, line 16, with the following redlined paragraph:

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% ~~Tween~~ TWEEN® 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

Please replace the paragraph beginning at page 85, line 4, with the following redlined paragraph:

Immunomagnetic beads coated with specific monoclonal antibodies to surface cell markers, or tetrameric antibody complexes, may be used to first enrich or positively select cancer cells in a sample. Various commercially available kits may be used, including

~~Dynabeads~~DYNABEADS® Epithelial Enrich (Dynal Biotech, Oslo, Norway), ~~StemSep~~STEMSEP®™ (StemCell Technologies, Inc., Vancouver, BC), and ~~RosetteSep~~ ROSETTESEP® (StemCell Technologies). A skilled artisan will recognize that other methodologies and kits may also be used to enrich or positively select desired cell populations. ~~Dynabeads~~DYNABEADS® Epithelial Enrich contains magnetic beads coated with mAbs specific for two glycoprotein membrane antigens expressed on normal and neoplastic epithelial tissues. The coated beads may be added to a sample and the sample then applied to a magnet, thereby capturing the cells bound to the beads. The unwanted cells are washed away and the magnetically isolated cells eluted from the beads and used in further analyses.

Please replace the paragraph beginning at page 85, line 17, with the following redlined paragraph:

ROSETTESEP® ~~RosetteSep~~ can be used to enrich cells directly from a blood sample and consists of a cocktail of tetrameric antibodies that targets a variety of unwanted cells and crosslinks them to glycophorin A on red blood cells (RBC) present in the sample, forming rosettes. When centrifuged over Ficoll, targeted cells pellet along with the free RBC. The combination of antibodies in the depletion cocktail determines which cells will be removed and consequently which cells will be recovered. Antibodies that are available include, but are not limited to: CD2, CD3, CD4, CD5, CD8, CD10, CD11b, CD14, CD15, CD16, CD19, CD20, CD24, CD25, CD29, CD33, CD34, CD36, CD38, CD41, CD45, CD45RA, CD45RO, CD56, CD66B, CD66e, HLA-DR, IgE, and TCR□□.

Please replace the paragraph beginning at page 88, line 24, with the following redlined paragraph:

Sera from adult patients with *de nova* AML or CML were studied for the presence of WT1 specific Ab. Recombinant proteins were adsorbed to TC microwell plates (Nunc, Roskilde, Denmark). Plates were washed with PBS/0.5%~~Tween~~ TWEEN® 20 and blocked with 1% BSA/PBS/0.1% TWEEN®~~Tween~~ 20. After washing, serum dilutions were added and incubated overnight at 4°C. Plates were washed and Donkey anti-human IgG-HRP secondary

antibody was added (Jackson-Immunochem, West Grove, PA) and incubated for 2h at room temperature. Plates were washed, incubated with TMB Peroxidase substrate solution (Kirkegaard and Perry Laboratories, MA), quenched with 1N H_2SO_4, and immediately read (Cyto-Fluor 2350; Millipore, Bedford, MA).

Please replace the paragraph beginning at page 91, line 1, with the following redlined paragraph:

Detection of existent antibodies to WT1 in patients with leukemia strongly implied that it is possible to immunize to WT1 protein to elicit immunity to WT1. To test whether immunity to WT1 can be generated by vaccination, mice were injected with TRAMP-C, a WT1 positive tumor cell line of B6 origin. Briefly, male B6 mice were immunized with 5 x 10^6 TRAMP-C cells subcutaneously and boosted twice with 5 x 10^6 cells at three week intervals. Three weeks after the final immunization, sera were obtained and single cell suspensions of spleens were prepared in RPMI 1640 medium (GIBCO®) with 25μM β-2-mercaptoethanol, 200 units of penicillin per ml, 10mM L-glutamine, and 10% fetal bovine serum.

Please replace the paragraph beginning at page 93, line 7, with the following redlined paragraph:

B6 mice were immunized with a group of WT1 peptides or with a control peptide. Peptides were dissolved in 1ml sterile water for injection, and B6 mice were immunized 3 times at time intervals of three weeks. Adjuvants used were CFA/IFA, GM-CSF, and ~~Montinide~~MONTANIDE®. The presence of antibodies specific for WT1 was then determined as described in Examples 1 and 2, and proliferative T cell responses were evaluated using a standard thymidine incorporation assay, in which cells were cultured in the presence of antigen and proliferation was evaluated by measuring incorporated radioactivity (Chen et al., *Cancer Res. 54*:1065-1070, 1994). In particular, lymphocytes were cultured in 96-well plates at $2x10^5$ cells per well with $4x10^5$ irradiated (3000 rads) syngeneic spleen cells and the designated peptide.

Please replace the paragraph beginning at page 131, line 1, with the following redlined paragraph:

Peptide binding to C57Bl/6 murine MHC was confirmed using the leukemia cell line RMA-S, as described by Ljunggren et al., *Nature 346*:476-480, 1990. In brief, RMA-S cells were cultured for 7 hours at 26°C in complete medium supplemented with 1% FCS. A total of 10^6 RMA-S cells were added into each well of a 24-well plate and incubated either alone or with the designated peptide (25ug/ml) for 16 hours at 26°C and additional 3 hours at 37°C in complete medium. Cells were then washed three times and stained with fluorescein isothiocyanate-conjugated anti D^b or anti-K^b antibody (PharMingen, San Diego, CA). Labeled cells were washed twice, resuspended and fixed in 500ul of PBS with 1% paraformaldehyde and analyzed for fluorescence intensity in a flow cytometer (Becton-Dickinson ~~FACSCalibur~~FACSCALIBUR™). The percentage of increase of D^b or K^b molecules on the surface of the RMA-S cells was measured by increased mean fluorescent intensity of cells incubated with peptide compared with that of cells incubated in medium alone.

Please replace the paragraph beginning at page 135, line 6, with the following redlined paragraph:

Mononuclear cells were isolated by density gradient centrifugation, and were immediately frozen and stored at -80°C until analyzed by RT-PCR for the presence of WT1 specific mRNA. RT-PCR was generally performed as described by Fraizer et al., *Blood 86*:4704-4706, 1995. Total RNA was extracted from 10^7 cells according to standard procedures. RNA pellets were resuspended in 25 µL diethylpyrocarbonate treated water and used directly for reverse transcription. The zinc-finger region (exons 7 to 10) was amplified by PCR as a 330 bp mouse cDNA. Amplification was performed in a thermocycler during one or, when necessary, two sequential rounds of PCR. ~~AmpliTaq~~ AMPLITAQ® DNA Polymerase (Perkin Elmer Cetus, Norwalk, CT), 2.5 mM $MgCl_2$ and 20 pmol of each primer in a total reaction volume of 50µl were used. Twenty µL aliquots of the PCR products were electrophoresed on 2% agarose gels stained with ethidium bromide. The gels were photographed with ~~Polaroid~~ POLAROID® film (Polaroid 667, Polaroid Ltd., Hertfordshire, England). Precautions against cross contamination

were taken following the recommendations of Kwok and Higuchi, *Nature 339*:237-238, 1989. Negative controls included the cDNA- and PCR-reagent mixes with water instead of cDNA in each experiment. To avoid false negatives, the presence of intact RNA and adequate cDNA generation was evaluated for each sample by a control PCR using β-actin primers. Samples that did not amplify with these primers were excluded from analysis.

Please replace the paragraph beginning at page 142, line 12, with the following redlined paragraph:

The PCR products were digested with EcoRI and cloned into pPDM His (a modified pET28 vector with a His tag in frame on the 5′ end) which has been digested with Eco72I and EcoRI. The constructs were confirmed to be correct through sequence analysis and transformed into BL21 pLys S and ~~BL21~~ BL21-~~CodonPlus~~ CODONPLUS® cells or BLR pLys S and BL21-CODONPLUS® ~~BLR CodonPlus~~ cells.

Please replace the paragraph beginning at page 143, line 10, with the following redlined paragraph:

The PCR product was digested with EcoRI and cloned into pPDM His which had been digested with Eco72I and EcoRI. The sequence was confirmed through sequence analysis and then transformed into BLR pLys S and BLR which is co-transformed with CODONPLUS® ~~CodonPlus~~-RP.

Please replace the paragraph beginning at page 145, line 13, with the following redlined paragraph:

The PCR product was digested with EcoRI and cloned into pPDM His which had been digested with Eco72I and EcoRI. The sequence was confirmed and then transformed into BLR pLys S and BLR which is co-transformed with CODONPLUS® ~~CodonPlus~~-RP.

Please replace the table beginning at page 146, line 20, with the following redlined table:

Table L

Experimental Design of WT1 Immunization in Mice

Histology Group	Corixa Group	Treatment Description	Dose Level	Total No. (Females)
1	0	No treatment	0	4
2	1.1	MPL®-SE (adjuvants alone), 6x, 1 week apart	10ug	4
3	1.2	MPL®-SE, 3x, 2 weeks apart	10ug	4
4	2.1	Ra12-WT1+ MPL®-SE, 6x	25ug	4
5	2.2	Ra12-WT1 + MPL®-SE, 3x	25ug	4
6	3.1	Ra12-WT1 + MPL®-SE, 6x	100ug	4
7	3.2	Ra12-WT1 + MPL®-SE, 3x	100ug	4
8	4.1	Ra12-WT1 + MPL®-SE, 6x	1000ug	4
9	4.2	Ra12-WT1 + MPL®-SE, 3x	1000ug	4

Please replace the paragraph beginning at page 147, line 2, with the following redlined paragraph:

Vaccination to WT1 protein using MPL®-SE as adjuvant, in a multiple dose titration study (doses ranging from 25μg, 100μg to 1000μg WT1 protein) in female C57/B6 mice elicited a strong WT1-specific antibody response (Figure 19) and cellular T-cell responses (Figure 20).

Please replace the paragraph beginning at page 156, line 3, with the following redlined paragraph:

Recombinant Ra12-WT1 concentration: 0.5 – 1.0 mg/ml; Buffer: 10-20 mM Ethanolamine, pH 10.0; 1.0 – 5.0 mM Cysteine; 0.05 % ~~Tween~~TWEEN®-80 (Polysorbate-80);

Sugar: 10% Trehalose (T5251, Sigma, MO) 10% Maltose (M9171, Sigma, MO) 10% Sucrose (S7903, Sigma, MO) 10% Fructose (F2543, Sigma, MO) 10% Glucose (G7528, Sigma, MO).

Please replace the paragraph beginning at page 156, line 17, with the following redlined paragraph:

According to this example, WT1 protein in combination with MPL®-SE induces a strong Ab and Interferon-γ (IFN-γ) response to WT1. Described in detail below are the methods used to induce WT1 specific immune responses following WT1 protein immunization using MPL®-SE or ~~Enhanzyn~~ENHANZYN® as adjuvant in C57/B6 mice.

Please replace the paragraph beginning at page 156, line 22, with the following redlined paragraph:

C57BL/6 mice were immunized with 20 μg rRa12-WT1 combined with either MPL®-SE or ENHANZYN® ~~Enhanzyn~~ adjuvants. One group of control mice was immunized with rRa12-WT1 without adjuvant and one group was immunized with saline alone. Three intramuscular (IM) immunizations were given, three weeks apart. Spleens and sera were harvested 2 weeks post-final immunization. Sera were analyzed for antibody responses by ELISA on plates coated with Ra12-WT1 fusion, Ra12 or WT1TRX. Similar levels of IgG2a and IgG1 antibody titers were observed in mice immunized with Ra12-WT1+MPL®-SE and Ra12-WT1+~~Enhanzyn~~ENHANZYN®. Mice immunized with rRa12-WT1 without adjuvant showed lower levels of IgG2a antibodies.

Please replace the paragraph beginning at page 157, line 3, with the following redlined paragraph:

CD4 responses were assessed by measuring Interferon-γ production following stimulation of splenocytes *in vitro* with rRa12-WT1, rRa12 or with WT1 peptides p6, p117 and p287. Both adjuvants improved the CD4 responses over mice immunized with rRA12-WT1 alone. Additionally, the results indicate that rRA12-WT1+MPL®-SE induced a stronger CD4 response than did rRA12-WT1+~~Enhanzyn~~ENHANZYN®. IFN-γ OD readings ranged from 1.4-

1.6 in the mice immunized with rRA12-WT1+MPL®-SE as compared to 1-1.2 in the mice immunized with rRA12-WT1+~~Enhanzyn~~ENHANZYN®. Peptide responses were only observed against p117, and then only in mice immunized with rRa12-WT1+MPL®-SE. Strong IFN-γ responses to the positive control, ConA, were observed in all mice. Only responses to ConA were observed in the negative control mice immunized with saline indicating that the responses were specific to rRA12-WT1.

Please replace the paragraph beginning at page 167, line 1, with the following redlined paragraph:

Total mRNA from 2 x 10^6 cells from a WT1 specific CD8+ T cell clone is isolated using ~~Trizol~~ TRIZOL® reagent and cDNA is synthesized using ~~Ready-to-go~~READY-TO-GO® kits (Pharmacia). To determine Vα and Vβ sequences in a clone, a panel of Vα and Vβ subtype specific primers are synthesized (based on primer sequences generated by Clontech, Palo Alto, CA) and used in RT-PCR reactions with cDNA generated from each clone. The RT-PCR reactions demonstrate which Vβ and Vα sequence is expressed by each clone.

Please replace the paragraph beginning at page 178, line 8, with the following redlined paragraph:

Three groups of A2/Kb mice were then immunized 3 times, 2 weeks apart as follows:

Group 1: saline alone s.c.(control, n=10 mice)

Group 2: MPL®-SE 10 μg alone s.c. (control, n=10 mice)

Group 3: Ra12/WT1 protein 100 μg + 10 μg MPL®-SE s.c. (n=9 mice)

Two to three weeks after the last WT1 immunization, mice were inoculated with 2 X 10^6 A2/Kb DC2.4 tumor cells overexpressing WT1. After tumor challenge mice were monitored and tumor size measured twice per week up to 4 weeks after tumor challenge.

Please replace the paragraph beginning at page 178, line 17, with the following redlined paragraph:

The results showed that the percentage of mice with tumor growth in the group that received the WT1 protein vaccine was reduced from about 100% (saline control) or 90% (MPL®-SE adjuvant control) to 45% (WT1 protein immunized group). Further, the average tumor volume was reduced in this group from an average tumor size of 1233 cmm (saline control) or 753cmm (MPL®-SE adjuvant control) observed in the control group to 226 cmm in the WT1 protein immunized group. Histopathological analyses showed that tumor margins in vaccinated animals were mixed with host immunological reactions including histiocytes, eosinophils, lymphocytes, mast cells and plasmacytes. Taken together, the results demonstrate that WT1 protein immunization protects against or delays the growth of WT1-positive tumors in the animals immunized with WT1. Thus, these results support the use of WT1 protein as a vaccine for malignancies associated with WT1 expression.

Please replace the paragraph beginning at page 180, line 8, with the following redlined paragraph:

WT-1-F (a.a. 2-281 of the WT1 protein; cDNA and amino acid sequence of 2-281 of WT1 are set forth in SEQ ID NOs:460 and 461, respectively) and full-length WT-1 were constructed as pTAT fusions with no His tag as described below. The cDNA sequence of the resulting fusion contructs pTAT-WT1F and the pTAT-WT1 full-length are set forth in SEQ ID NOs 452 and 453 respectively. The~~and~~ amino acid sequences of the resulting fusions are set forth in ~~SEQ ID NOs:452 and 453 and~~ SEQ ID NOs:~~454~~ 455 and ~~455~~454, respectively.

Please replace the paragraph beginning at page 181, line 16, with the following redlined paragraph:

In this Example, mice were immunized with different protein constructs of WT-1, (F truncation (2-281) and full length (2-430) as described in Example 34)) formulated with MPL®-SE adjuvant. Improved CD4 responses were elicited by the truncated constructs relative to the full length protein. Thus, this example demonstrates that the N-terminal portion of the

WT1 protein spanning from amino acid 2 to 281 is the dominant immunogenic portion of the WT1 protein *in vivo*.